ISSN 0975 -8542

Journal of Global Pharma Technology

Available Online at www.jgpt.co.in

REVIEW PAPER

A Systematic Review of Iranian Medicinal Plants Effective on Female Infertility

Majid Shirani[1], Sheida Shabanian[2], Mahnaz Yavangi[3]*

[1]*Cellular and Molecular Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.*

[2]*Medicinal Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran;*

[3]*Department of Gynecology, Endometrium and Endometriosis Research Center, Hamadan University of Medical Sciences, Hamadan, Iran.*

*Corresponding Author: **Mahnaz Yavangi**

Abstract: Infertility is one of the common and rising problems of women. To treat female infertility, medicinal plants may be used in addition to chemical drugs and assisted reproductive technology. To conduct this review, the terms *Fertility* and *Pregnancy* in combination with *Medicinal plants*, *Herb*, and *Phyto* were used to search for and retrieve relevant publications indexed in international databases ISI and PubMed and domestic databases Iran Medex and ISC. The articles that fulfilled the inclusion criteria were analyzed. In this systematic review article, the medicinal plants that were found to be effective on female infertility indices were reported. These plants, according to this review article, are *Nigella sativa*, *Panax ginseng*, *Phoenix dactylifera* L., salep, *Glycyrrhiza glabra*, *Apium graveolens* L., and *Foeniculum vulgare* Mill. The medicinal plants used by Iranian people have been reported to exert optimal effects on female fertility in animal studies through antioxidant properties, increasing follicogenesis, hormonal compounds, and other effective compounds on hormonal system as well as enhancing sex cells viability.

Keywords: *Infertili1ty, Female, Medicinal plants, Iran.*

Introduction

The prevalence of infertility is on rise in different countries including Iran (1, 2). Female infertility is due to several reasons such as obesity (3), infection (4), diabetes (5), and hypothyroidism (6) and may be associated with certain factors including physical inactivity, the number of abortions, and lifestyle (7). Treatment cycles of infertility such as in vitro fertilization and use of chemical drugs cause certain complications and high levels of psychological and emotional stress for the patients in addition to imposing stupendous costs (8, 9). For several reasons, treatments for infertility may be unsuccessful and associated problems of the patients can be considerably intensified (2). Besides that, infertile women in Iran experience certain social problems such as stigma and social exclusion that affect their quality of life adversely (10). Therefore, attempts are continuously made to enhance and develop alternative therapies for infertility.

Plant-based treatments for infertility can increase fertility in infertile women even by 100% regarding effective factors on infertility (3, 4). Medicinal plants and nature-based compounds have recently been commonly used to treat different diseases because of fewer side effects (11-22). However, use of complementary therapies and medicinal plants to treat infertility is still controversial (5). Medicinal plants have been found to be potential appropriate alternative therapies for infertility (6). This

systematic review was conducted to assess the medicinal plants effective on female infertility indices. This review article can help provide new pharmaceutical compounds for researchers and pharmacists to produce effective herbal drugs on female infertility.

To conduct this review, the terms *Fertility* and *Pregnancy* in combination with *Medicinal plants*, *Herb*, and *Phyto* were used to search for and retrieve relevant publications indexed in international databases ISI and PubMed and domestic databases Iran Medex and ISC. Then, the abstracts and data drawn from other resources were examined and only those studies that were conducted mainly to investigate the effects of the plants and their derivatives on female infertility in Iran and on medicinal plants native to Iran were included in analysis.

Results

Nigella sativa, ginseng, *Aloe vera*, *Phoenix dactylifera* L., salep, *Glycyrrhiza glabra*, *Apium graveolens* L., *Foeniculum vulgare* Mill., *Allium sativum*, *Vitex agnus-castus* L., and *Portulaca oleracea* have been reported to be used to increase female infertility in Iran according to traditional medicine (23); however, only *N. sativa*, ginseng, *P. dactylifera*, salep, *G. glabra*, *A. graveolens*, and *F. vulgare* were studied in experimental works with animals.

N. Sativa

N. sativa is an annual flowering plant that produces black seeds and is from family Ranunculaceae (24). Hydroalcoholic *N. sativa* seed extract causes increase in follicogenesis and corpus luteum, which can be due to the optimal outcome in female fertility (25).

Panax Ginseng

A study demonstrated that treatment with vitamin E and ginseng caused increase in the number of laboratory pregnant mice and babies born due to inducing antioxidant property in sex cells (26).

Date Palm Pollen (*P. Dactylifera* L.)

A study demonstrated that 400 mg/kg *P. dactylifera* pollen extract caused increase in the levels of sex hormones and the number of secondary and anthral follicles in adult female BALB/c mice (27). This extract increases female fertility in BALB/c mice through stimulating follicogenesis (28).

Salep

A study indicated that aqueous salep root extract caused significant modulation of serum FSH and increase in serum estrogen in female rats (29).

G. Glabra

G. glabra is from family Leguminosae. Aqueous *G. glabra* extract was reported to be effective on the levels of sex hormones and cause increase in the in vitro maturity of the oocytes and in vitro fertility in laboratory mice with polycystic ovary syndrome (30).

F. Vulgare

A study on the effects of *Cichorium intybus*, *F. vulgare*, and *A. graveolens* on fertility and infant gender in rats demonstrated that *F. vulgare* caused increase in fertility and the number of the infants (31). Another study demonstrated that alcoholic *F. vulgare* seed extract caused stimulation of follicogenesis in mouse ovaries, which is due to its estrogenic property (32). Study of serum levels of estrogen, progesterone, and prolactin in female mice demonstrated that *F. vulgare* was effective in increasing the serum levels of these hormones and could be used as a drug for infertility (33).

A. Graveolens

A. graveolens caused increase in the number of babies in female mice due to several flavonoids such as quercetin and cytosterol, phytoesterol, and antioxidants that are usually produced from protein. Therefore, hydroalcoholic *A. graveolens* leaf extract is effective in increasing fertility indices in female mice but causes reduction in weight of their infants (34).

This study was conducted to investigate the plants and plant-based compounds that are effective on female infertility. In the previous studies, oxidative stress has been reported to be a reducing agent of fertility. The studied plants have been found to increase fertility due to antioxidant properties (35, 36). Also natural antioxidants can be effective in prevention of various diseases (37-48). However, an important

point which should be seriously considered is that gynecological oxidative stress is an important mediator of conception, but higher than threshold levels of oxidative stress cause toxic effects and challenge conception. This issue, however, is dependent on the stage of preconception and anatomic location (49, 50).

Therefore, ovulation, administered dose, nutritional factors, and other confounders are issues that have been less frequently investigated (51-53), which challenge the available findings. According to reviewed studies in laboratory female animals, some plants exert their effects due in different mechanisms (Figure 1).

Figure 1: Several mechanisms herbal medicine to increase fertility

However, certain plants that have phytoestrogenic properties and therefore cause hormonal changes in females are likely to prevent fertility in males. For example, hydroalcoholic *F. vulgare* extract has been demonstrated to reduce male fertility (54, 55).

Besides that, some plants increase fertility in both genders. *P. dactylifera* pollen, *Panax ginseng*,extract, and *A. graveolens* extract are certain plant-based compounds that enhance fertility indices in both females (26, 27, 34) and males (26, 56-59). In addition, the teratogenic properties of the compounds of the plants that are used to increase female infertility should be taken into account. As a result, such plants should be used in the light of necessary precautions and under supervision of specialists.

Conclusion

Several plants are used to treat infertility in Iran a small number of which have already been investigated in experimental studies. These plants cause promotion of fertility indices through inducing antioxidant property in the tissues and reproductive organs of females as well as activating gonads due to phytochemicals and pseudohormonal compounds. In addition, they stimulate follicogenesis and increase healthy sex cells.

References

1. Kazemijaliseh H, Ramezani Tehrani F, Behboudi-Gandevani S, Hosseinpanah F, Khalili D, Azizi F (2015) The prevalence and causes of primary infertility in Iran: A population-based study. Glob J Health Sci. 7(6):226-32.
2. Akhondi MM, Kamali K, Ranjbar F, Shirzad M, Shafeghati S, Behjati Ardakani Z,(2013) et al. Prevalence of primary infertility in Iran in 2010. Iranian Journal of Public Health. 42(12):1398-404.
3. Zain MM, Norman RJ (2008) Impact of obesity on female fertility and fertility treatment. Women's health (London, England). 4(2):183-94.
4. Rodriguez R, Hernandez R, Fuster F, Torres A, Prieto P, Alberto J (2001) [Genital infection and infertility]. Enfermedades infecciosas y microbiologia clinica. 19(6):261-6.
5. Livshits A, Seidman DS (2009) Fertility issues in women with diabetes. Women's health (London, England). 5(6):701-7.
6. Verma I, Sood R, Juneja S, Kaur S (2012) Prevalence of hypothyroidism in infertile women and evaluation of response of

treatment for hypothyroidism on infertility. International Journal of Applied and Basic Medical Research 2(1):17-9.

7. Cong J, Li P, Zheng L, Tan J (2016) Prevalence and Risk Factors of Infertility at a Rural Site of Northern China. PloS one. 11(5):e0155563.
8. Katz P, Showstack J, Smith JF, Nachtigall RD, Millstein SG, Wing H,(2011) et al. Costs of infertility treatment: Results from an 18-month prospective cohort study. Fertility and sterility. 95(3):915-21.
9. Hasanpoor-Azghdy SB, Simbar M, Vedadhir A (2014) The emotional-psychological consequences of infertility among infertile women seeking treatment: Results of a qualitative study. Iranian Journal of Reproductive Medicine. 12(2):131-8.
10. Hasanpoor-Azghdy SB, Simbar M, Vedadhir A (2015) The Social Consequences of Infertility among Iranian Women: A Qualitative Study. International Journal of Fertility & Sterility. 8(4):409-20.
11. Asadi-Samani M, Kooti W, Aslani E, Shirzad HA (2016) systematic review of Iran's medicinal plants with anticancer effects. Journal of evidence-based complementary & alternative medicine. 21(2):143-53.
12. Sani MRM, Asadi-Samani M, Saeedi-Boroujeni A, Banitalebi-Dehkordi M, Bahmani M (2016) Suppressive effects of medicinal plants and their derivatives on inflammasome complex: A systematic review. International Journal of PharmTech Research. 9(6):325-35.
13. Parsaei P, Bahmani M, Karimi M, Naghdi N, Asadi-Samani M, Rafieian-Kopaei MA (2016) review of analgesic medicinal plants in Iran. Der Pharmacia Lettre. 8(2):43-51.
14. Bahmani M, Tajeddini P, Ezatpour B, Rafieian-Kopaei M, Naghdi N, Asadi-Samani M (2016) Ethenobothanical study of medicinal plants against parasites detected in Shiraz, southern part of Iran. Der Pharmacia Lettre. 8(1):153-60.
15. Parsaei P, Bahmani M, Naghdi N, Asadi-Samani M, Rafieian-Kopaei M (2016) The most important medicinal plants effective on constipation by the ethnobotanical documents in Iran: A review. Der Pharmacia Lettre. 8(2):188-94.
16. Jivad N, Asadi-Samani M, Moradi MT (2016) The most important medicinal plants effective on migraine: A review of ethnobotanical studies in Iran. Der Pharma Chemica. 8(2):462-6.
17. Jivad N, Bahmani M, Asadi-Samani M (2016) A review of the most important medicinal plants effective on wound healing on ethnobotany evidence of Iran. Der Pharmacia Lettre. 8(2):353-7.
18. Parsaei P, Bahmani M, Naghdi N, Asadi-Samani M, Rafieian-Kopaei M, Boroujeni S (2016) Shigellosis phytotherapy: A review of the most important native medicinal plants in Iran effective on Shigella. Der Pharmacia Lettre.;8(2):249-55.
19. Raeisi E, Shahbazi-Gahrouei D, Heidarian E (2016) Pineapple extract as an efficient anticancer agent in treating human cancer cells. Front Cancers. 1(1):03.
20. Nasri H. Herbs hazards (2017) administration of herbal drugs in maintenance hemodialysis patients. Ann Res Dial. ;2(1):01.
21. Bahmani M, Asadi-Samani M (2016) Native medicinal plants of Iran effective on peptic ulcer. Journal of Injury and Inflammation. 1(1):e05.
22. Rafieian-Kopaei M (2013) Medicinal plants for renal injury prevention. J Renal Inj Prev. 2(2):63-5.
23. Shabanian S, Bahmani M, Asadi-Samani M (2016) The medicinal plants effective on female hormones: A review of the native medicinal plants of Iran effective on estrogen, progesterone, and prolactin. Journal of Chemical and Pharmaceutical Sciences. 9(3):1270-6.
24. Kooti W, Hasanzadeh-Noohi Z, Sharafi-Ahvazi N, Asadi-Samani M, Ashtary-Larky D (2016) Phytochemistry, pharmacology, and therapeutic uses of black seed (Nigella sativa). Chinese Journal of Natural Medicines. 14(10):732-45.
25. Modaresi M, Poor-Naji n (2012) The effect of black seed (Nigella sativa) hydro-alcoholic extract on breeding factors in female mice. Journal of Shahrekord Uuniversity of Medical Sciences. 13(6):63-70.
26. Hosseini A, Zare S, Ghaderipakdel F, Ahmadi (2010) A Evaluate the antioxidant effect of ginseng extract and vitamin E on fertility Laboratory male rats after long-

term treatment with cyclophosphamide. Quarterly of Reproduction and Infertility. 11(4):227-37.

27. Hosseini E, Mehrabani D, Razavi f (2014) Effect of palm pollen extract on sexual hormone levels and follicle numbers in adult female BALB/c mice. Quarterly of Horizon of Medical Sciences. 20(3):139-43.
28. Moshfegh F, Baharara J, Namvar F, Zafar-Balanezhad S, Amini E, Jafarzadeh L (2016) Effects of date palm pollen on fertility and development of reproductive system in female Balb/C mice. Journal of Herbmed Pharmacology.;5(1):23-8.
29. Kargar jahromi h, solhjo k, solhjo ka, Kargar jahromi z, ebrahimian a (2015) The effect of aqueous extract of the roots of Salep plants on the serum concentration of FSH and estrogen hormone in female rats. Pars of Jahrom University of Medical Sciences. 13(2):0-.
30. Shamsi M, Nejati V, Najafi G (2016) Therapeutic Effects of Licorice Extract on In vitro Maturation and In vitro Fertilization in Mice Model of Polycystic Ovary Syndrome. Journal of Mazandaran University of Medical Sciences. 25(132):113-21.
31. Fallah Huseini H, Kianbakht S (2012) Study on Effects of Chicory (Cichorium intybus L.), Fennel (Foeniculum vulgare Mill.) and Dill (Anethum graveolens L.) on Fertility and Neonatal Gender in Rats. Journal of Medicinal Plants.;2(42):192-6.
32. Khazaei M, Montaseri A, Khazaei MR, Khanahmadi M (2011) Study of Foeniculum vulgare Effect on Folliculogenesis in Female Mice. International Journal of Fertility & Sterility. 5(3):122-7.
33. Sadeghpour N, Khaki AA, Najafpour A, Dolatkhah H, Montaseri A (2015) Study of Foeniculum vulgare (Fennel) Seed Extract Effects on Serum Level of Estrogen, Progesterone and Prolactin in Mouse. A General Policy. 2:23-7.
34. Kooti W, Ghasemiboroon M, Asadi-Samani M, Ahangarpoor A, Zamani M, Amirzargar A,(2014) et al. The effect of halcoholic extract of celery leaves on the delivery rate (fertilization and stillbirths), the number, weight and sex ratio of rat off spring. Advances in Environmental Biology. 824-31.
35. Kooti W, Ghasemiboroon M, Ahangarpoor A, Hardani A, Amirzargar A, Asadi-Samani M,(2014) et al. The Effect of Hydro-Alcoholic Extract of Celery on Male Rats in Fertility Control and Sex Ratio of Rat Offspring. J Babol Univ Med Sci.;16(4):43-9.
36. Mansori E, Ghasemiboroon M, Samani MA, Alamiri F, Ashtari D, Kafash Farkhad N,(2016) et al. The effect of hydro-alcoholic extract of Apium graveolens L. leaf on delivery rate in female rats, and weight and gender ratio of infants. Jundishapur J Nat Pharm Prod.: inpress:e28802.
37. Baradaran A(2017) Herbal antioxidant to ameliorate vascular biology. Angiol Persica Acta.;2(1):e01.
38. Ghatreh-Samani M, Esmaeili N, Soleimani M, Asadi-Samani M, Ghatreh-Samani K, Shirzad H(2016) Oxidative stress and age-related changes in T cells: is thalassemia a model of accelerated immune system aging? Central-European journal of immunology. 41(1):116-24.
39. Hajian S (2015) Positive effect of antioxidants on immune system. Immunopathol Persa. 1(1):e02.
40. Khodadadi S, Rafieian-Kopaei M (2016) Herbs, health and hazards; a nephrology viewpoint on current concepts and new trends. Annals of Research in Antioxidants.;1(1):e05.
41. Mohammadparast V(2016) Antioxidant efficacy of Hibiscus esculentus. Front Biomed. 1(1):e04.
42. Nasri P (2017) Cancers and herbal antioxidants. Front Biomark.;2(1):e01.
43. Rafieian-Kopaei M, Baradaran A, Rafieian M.(2013) Plants antioxidants: From laboratory to clinic. J Nephropathol.;2(2):152-3. doi: 10.12860/JNP.2013.26.
44. Nasri H, Abedi-Gheshlaghi Z, Rafieian-Kopaei M (2016) Curcumin and kidney protection; current findings and new concepts. Acta Persica Pathophysiologica.;1(1):e01.
45. Dehghan Shahreza F (2016) Hibiscus esculentus and diabetes mellitus. Journal of nephropharmacology.;5(2):104-5.
46. Kafeshani M (2015) Ginger, micro-inflammation and kidney disease. Journal of Renal Endocrinology.;1(1):e04.
47. Baradaran A (2017) Administration of herbal drugs in geriatric individuals;

trends on its helps and hazards. Geriatr Persia.;1(1):e01.

48. Nasri H (2017) Herbal drugs; from molecular studies to bedside investigations. Aria J Front Biochem.;2(1):e01.
49. Ruder EH, Hartman TJ, Blumberg J, Goldman MB (2008) Oxidative stress and antioxidants: exposure and impact on female fertility. Human reproduction update.;14(4):345-57.
50. Ruder EH, Hartman TJ, Goldman MB (2009) Impact of oxidative stress on female fertility. Current opinion in obstetrics & gynecology.;21(3):219-22.
51. Nejatbakhsh F, Nazem E, Goushegir A, Isfahani MM, Nikbakht Nasrabadi A, Baygom Siahpoosh M (2012) Recommended foods for male infertility in Iranian traditional medicine. Iranian Journal of Reproductive Medicine.;10(6):511-6.
52. Zhang Y, Fu Y, Han F, Kuang H, Hu M, Wu X (2014) The Effect of Complementary and Alternative Medicine on Subfertile Women with In Vitro Fertilization. Evidence-based Complementary and Alternative Medicine : eCAM.;2014:419425.
53. Lyttleton J (2013) Treatment of infertility with Chinese medicine: Elsevier Health Sciences;.
54. Mansouri E, Asadi-Samani M, Kooti W, Ghasemiboroon M, Ashtary-Larky D, Alamiri F (2016) , et al. Anti-fertility effect of hydro-alcoholic extract of fennel (Foeniculum vulgare Mill) seed in male Wistar rats. Journal of Veterinary Research.;60(3):357-63.
55. Dehghani F, Panjehshahin M, Mirzaee Z, Mehrabani D (2005) Effect of Foeniculum vulgare organic extract on blood sex hormones and reproductive tissues of male rats. Journal of Applied Animal Research.;27(1):17-20.
56. Hardani A, Afzalzadeh MR, Amirzargar A, Mansouri E, Meamar Z (2015) Effects of aqueous extract of celery (Apium graveolens L.) leaves on spermatogenesis in healthy male rats. Avicenna J Phytomed.;5(2):113-9.
57. Kooti W, Mansouri E, Ghasemiboroon M, Harizi M, Ashtary-Larky D, Afrisham R(2014) The Effects of Hydroalcoholic Extract of Apium graveolens Leaf on the Number of Sexual Cells and Testicular Structure in Rat. Jundishapur J Nat Pharm Prod.;9(4):e17532.
58. Modaresi M, Ghalamkari G, Jalalizand A (2012) The Effect of Celery (Apium graveolens) Extract on the Reproductive Hormones in Male Mice. Apcbee Proc.;4:99-104.
59. Rasekh A, Jashni HK, Rahmanian K, Jahromi AS (2015) Effect of Palm Pollen on Sperm Parameters of Infertile Man. Pak J Biol Sci.;18(4):196-9.

